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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/994,485	11/27/2001	Alexey G. Ryazanov	601-1-078DIV	1500

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David A. Jackson, Esq.
KLAUBER & JACKSON
411 Hackensack Avenue
Hackensack, NJ 07601

EXAMINER	
ANDRES, JANET L	
ART UNIT	PAPER NUMBER
1646	12

DATE MAILED: 01/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/994,485	RYAZANOV ET AL.	
	Examiner	Art Unit	
	Janet L Andres	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-59* is/are pending in the application.

4a) Of the above claim(s) *50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence alignments* .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group 2 in paper no. 11 is acknowledged. Claims 50-59 are pending in this application; claim 50 is withdrawn from consideration as being drawn to a non-elected invention. The restriction requirement of paper no. 7 is made FINAL. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

2. The abstract of the disclosure is objected to because it is an abstract of the invention, not the disclosure. Correction is required. See MPEP § 608.01(b).

The disclosure is objected to because of the following informalities: There are sequences on p. 14, line 1, p. 44, lines 11 and 12, and p. 54, line 4, that lack sequence identifiers. See MPEP §2421.02

Appropriate correction is required.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 51, 52, and 58 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims are drawn to antibodies or fragments of

antibodies that are not modified in any way from what would exist in nature. Antibodies to naturally-occurring proteins are found in nature (Harlow and Lane, Antibodies, 1988, pp. 2-3) and, since proteins are broken down and processed in nature, fragments of antibodies also occur naturally. Because the claims do not require that the antibodies be isolated, they encompass products of nature and thus are directed to non-statutory material.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 51 and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Redpath et al., J. Biol. Chem. 1996, vol. 271 (29), pp. 17547-17554.

Redpath et al. teaches anti-peptide antibodies that were raised against two peptides identified by partial sequencing of rabbit eEF-2 kinase (p. 17548, column 1). These antibodies reacted with rat eEF-2 kinase (p. 17548, column 2, and p. 17549, column 1, figure 2), which is 90% identical to instant SEQ ID NO: 2. Peptide 1 differs from the corresponding rat sequence and from the corresponding region of instant SEQ ID NO: 4 in one amino acid and from the corresponding region of SEQ ID NO: 2 in three amino acids; the remaining sequence of 14 amino acids is identical in the peptide, the rat sequence, the human sequence, and the mouse sequence (see attached sequence alignments). Thus, since antibodies raised against the rabbit peptide reacted with the rat protein, they would also react with the identical sequence in the mouse protein and the nearly identical sequence in the human protein, anticipating the limitations

of claims 51 and 52. Peptide 2 differs from the corresponding rat sequence in two amino acids, from SEQ ID NO: 4 in three amino acids, and from SEQ ID NO: 2 in two amino acids (see attached alignments). Thus, since antibodies raised against this sequence reacted with the rat protein, they would also react with the nearly identical sequences in the human and mouse proteins, and would also anticipate the limitations of claims 51 and 52.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 51 and 53-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Redpath et al. in view of Harlow and Lane, Antibodies, 1988.

Claims 53 and 54 are drawn to monoclonal antibodies and a cell line that produces such antibodies. Redpath et al. teaches anti-peptide polyclonal antibodies (p. 17548, column 2) but fails to teach monoclonal antibodies or immortal cell lines. Harlow and Lane teach means of generating monoclonal antibodies and generation of immortal cell lines; see pages 141-42.

Harlow and Lane fails to teach generation of monoclonal antibodies to the proteins taught by Redpath et al. However, it would be obvious to one of ordinary skill in the art to combine the teachings of Redpath et al. with those of Harlow and Lane to generate monoclonal antibodies to eEF-2 kinases. One of ordinary skill would have been motivated to do so because Redpath et al. teaches uses for antibodies (figures 2 and 6) and Harlow and Lane teaches that monoclonal antibodies are advantageous because they are specific and because they can be produced in unlimited amounts (p. 141).

Claims 55-57 are drawn to labeled antibodies. Redpath et al. teaches as set forth above but fails to teach detectable labels. Fluorescent, enzymatic, and radioactive labels are taught by Harlow and Lane in table 9.1 on p. 322. Harlow and Lane fails to teach labeling of the antibodies of Redpath et al. However, it would be obvious to one of ordinary skill in the art to label the antibodies of Redpath et al. as taught by Harlow and Lane. One of ordinary skill in the art would have been motivated to do so because Harlow and Lane teaches on p. 321 that such labeling is needed for a wide variety of immunological techniques. Thus one of ordinary skill would realize that labeling the antibodies would allow them to be used for additional purposes for which the unlabeled antibodies could not be used.

Claim 58 is drawn to antibody fragments. Redpath et al. teaches as set forth above but fails to teach fragments. Antibody fragments are taught by Harlow and Lane on p. 626. Harlow and Lane fails to teach fragments of the antibodies taught by Redpath et al. However, it would have been obvious to one of ordinary skill in the art to combine the teachings of Redpath et al. with those of Harlow and Lane to generate fragments of antibodies to eEF-2 kinase. One of ordinary skill would have been motivated to do so because Harlow and Lane teaches that such

fragments of advantages in techniques such as identification of antigens on cell surfaces. Thus, one of ordinary skill would expect such fragments to be useful for purpose for intact antibodies would be problematic.

Claim 59 is drawn to antibodies in pharmaceutical carriers. Redpath et al. teaches as set forth above but fails to teach pharmaceutically acceptable carriers. Harlow and Lane teaches that antibodies may be iodinated in phosphate buffered saline, which is a pharmaceutically acceptable carrier, on p. 336 and also teaches storage of antibodies in phosphate buffered saline on p. 287. Harlow and Lane fails to teach the antibodies taught by Redpath et al. in phosphate buffered saline. However, it would be obvious to one of ordinary skill in the art to suspend the antibodies taught by Redpath et al. in phosphate buffered saline for purposes of iodination or storage. One of ordinary skill would be motivated to do so because Harlow and Lane teaches that phosphate buffered saline can be used for these purposes.

Claims 51 and 53-59 encompass antibodies to the *c. elegans* sequence SEQ ID NO: 10 as well as the human and mouse sequences. Redpath et al. teaches a *c. elegans* protein in figure 7, p. 17553. This protein is identical to residues 1-415 and 500-768 of instant SEQ ID NO: 10. Thus, antibodies raised against this protein would react with the protein of instant SEQ ID NO: 10. Redpath et al. does not teach such antibodies. However, Harlow and Lane teaches techniques for selecting antigens for the generation of antibodies on pages 72-76. Harlow and Lane additionally teaches uses for antibodies such as cell staining (p. 361), immunoprecipitation (p. 423), immunoblotting (p. 473), purification (p. 513), and immunoassays (p. 555-556). While Harlow and Lane fail to teach antibodies to the *c. elegans* protein taught by Redpath et al., it would be obvious to one of ordinary skill in the art to generate such antibodies based on the

sequence disclosed by Redpath et al. One of ordinary skill would have been motivated to do so because Harlow and Lane teach many uses for such antibodies, and because Redpath et al. teach the use of antibodies to related proteins in figure 2, page 17549, and figure 6, page 17552. Thus, one of ordinary skill would expect, based on the teachings of Harlow and Lane, to be able to generate antibodies against the *c. elegans* protein, and would further expect that such antibodies would be useful for assays such as are taught by Harlow and Lane and particularly for the assays taught for antibodies to similar proteins by Redpath et al. It would further be obvious to one of ordinary skill in the art to generate monoclonal antibodies as claimed in claims 53 and 54 and to modify the antibodies as claimed in claims 55-59 for the reasons set forth above, that Harlow and Lane teaches the advantages of such procedures.

9. Claims 51-59 are rejected under 35 U.S.C. 103(a) as unpatentable over Ryazanov et al., Proc. Nat. Acad. Sci., May 1997, vol. 94, pp. 4884-4889, in view of Harlow and Lane, Antibodies, 1988.

Ryanazov et al. teaches human, mouse, and *c. elegans* eEF-2 kinases that are identical to instant SEQ ID NOS; 2, 4, and 10 in Figure 4, p. 4887. Ryanazov et al. does not teach antibodies to any of these sequences. As stated in paragraph 8 above, Harlow and Lane teaches techniques for selecting antigens for the generation of antibodies on pages 72-76 and teaches uses for such antibodies on pages 361, 423, 473, 513, and 555-556. While Harlow and Lane fail to teach antibodies to the proteins taught by Ryanazov et al., it would be obvious to one of ordinary skill in the art to generate such antibodies based on the sequences disclosed by Ryanazov et al. One of ordinary skill would have been motivated to do so because, as stated in paragraph 8, Harlow and Lane teaches that such antibodies are useful and one of ordinary skill would expect to be

able to generate such antibodies and would further expect that such antibodies could be used for the purposes taught by Harlow and Lane. It would further be obvious to one of ordinary skill in the art to generate monoclonal antibodies as claimed in claims 53 and 54 and to modify the antibodies as claimed in claims 55-59 for the reasons set forth above, that Harlow and Lane teach the advantages of such procedures.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 59 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman,* (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands,* 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

This claim is drawn to a pharmaceutical composition comprising an antibody to eEF-2 kinase. However, the specification teaches only that preliminary evidence indicates that eEf-2 kinase is upregulated in some cancers (p. 6, lines 2-4), and teaches on pages 29-31 that antibodies might be useful diagnostically. There are no teachings in the specification to indicate

for what cancers such antibodies could be used, and how the presence of eEF-2 kinase would correlate with disease and thus how the information obtained would be useful. On p. 29, lines 18-21, Applicant anticipates that "further experimentation will reveal a prognostic correlation between eEF-2 kinase levels and the prediction and or progression of certain malignancies". Thus what is presented is not a set of conditions for which the presence of the kinase would be diagnostic, but merely an invitation to the artisan to use the current invention as a starting point for further experimentation to identify such conditions. Without further guidance as to what conditions, if any, for which the presence of the kinase would be diagnostic, one of skill in the art could not predictably use the antibodies for a pharmaceutical purpose. Thus it would require undue experimentation to use the antibodies as pharmaceutical compositions.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 58 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This claim is drawn to an "active fragment" of an antibody. There is no definition in the specification of what activity the fragment is required to have. Thus, one of skill in the art would not be able to determine what activities, and thus what fragments, Applicant intended the claim to encompass.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
Patent Examiner

January 27, 2003